dilated left ventricular end-diastolic dimensions (average 70 mm). Hence, one should be careful when considering these results in the heart failure patients of New York Heart Association functional classes I and II.

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Redox Regulation of Post-Prandial Vascular Endothelial Dysfunction

Prophylactic Benefits of High-Intensity Exercise

Tyldum et al. (1) elegantly demonstrated that an acute bout of high-intensity interval exercise (HIE) provides superior prophylaxis against post-prandial vascular endothelial dysfunction compared with an isocaloric bout of continuous moderate-intensity exercise. The post-prandial maintenance of brachial artery flow-mediated vasodilation was attributed to an enhanced mobilization of antioxidants into the systemic circulation, which was shown to be exercise-intensity dependent. The authors speculated that by neutralizing lipemia-induced oxidative stress, HIE preserved endothelial function subsequent to an increase in vascular nitric oxide (NO) bioavailability. Given the limited assessment of free radical metabolism, I would like to raise some additional points for consideration and indeed proffer an alternative interpretation at least for their metabolic findings.

The authors referred to our study, which documented an exercise-induced mobilization of lipid soluble antioxidants into human skeletal muscle (2). Within the context of their observed HIE-induced increase in (blood borne) total antioxidant status, this was taken as evidence that "acute [HIE] exercise tends to tip the pro- and antioxidant balance in favor of increased antioxidant status." However, this interpretation is incorrect because multiple biomarkers of free radical–mediated lipid peroxidation, end point determinants of oxidative stress (regardless of the antioxidant response), were shown to increase markedly. Thus, the exercise-induced mobilization of antioxidants into both muscle and blood serves to limit, although clearly not terminate, oxidative stress, which, despite the body's best (antioxidant) efforts, ultimately prevails.

Furthermore, increased vascular lipid free radical formation does not necessarily translate into reduced endothelial NO bioavailability (3). Whether the observed elevation in total antioxidant status illustrated in Figure 2 of Tyldum et al. (1) (≈150 μmol compared with the continuous moderate-intensity exercise trial, which, in contrast, was characterized by impaired endothelial function) was sufficient to outcompete "inactivating species" such as superoxide ($O_2^{\cdot-} + NO^{\cdot} \rightarrow ONOO^-$, $k = \approx 10^9$ M/s) to liberate an "additional" pocket of (endothelial) NO is also from a thermodynamic standpoint questionable given the pharmacological concentrations of (for example) ascorbate required to achieve such an effect (>1 mM, which equates to roughly 20-fold the ambient plasma concentration). Finally, I would argue that it is the rate of antioxidant depletion that is more important than the absolute baseline concentration because it likely reflects the dynamics of consumption due to the sacrificial scavenging of free radicals. Thus, if anything, the HIE (and indeed the continuous moderate-intensity exercise) group exhibited a blunted antioxidant response compared with the control (no exercise) group.

Is it conceivable, given that the antioxidants were confined to the intravascular space, that the exercise intensity-dependent elevation in plasma total antioxidant status does not represent a priming of the body's endogenous antioxidant defenses but is merely a hemoconcentration artifact subsequent to plasma volume loss (4), further perpetuated by food intake? As little as 30 s of high-intensity exercise has been shown to depress plasma volume for as long as 24 h into recovery, which, incidentally, was associated with increased oxidative stress despite the blood's best efforts to elevate retinol and α-tocopherol (5). Although the superior cardioprotection afforded by HIE is indeed a fascinating and truly novel finding, further research is required to establish whether this is due to altered redox homeostasis.

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